**Evaluation of Sustained Release delivery Systems:**

Sustained release systems include any drug delivery system that achieves slow release of drug over an extended period of time. If the system is successful in maintaining constant drug levels in the blood or target tissue it is considered as controlled release system. If it is unsuccessful at this but nevertheless extends the duration of action over that achieved by conventional delivery, it is considered a prolonged release system. The oral route of administration for sustained release systems has received greater attention because of more flexibility in dosage form design. The design of oral sustained release delivery systems is subject to several inter related variables of considerable importance such as the type of delivery system, the disease being treated, the patient, the length of therapy and the properties of the drug.

Before marketing a sustained release product, it is must to assure the strength, safety, stability and reliability of a product by forming in-vitro and invivo analysis and correlation between the two. Various authors have discussed the evaluating parameters and procedures for sustained release formulations.

**1. In – Vitro Methods:**-

a. Beaker method

b. Rotating disc method

c. Rotating Bottle method

d. Rotating Basket method

e. Stationary Basket Method

f. Oscillating tube method

g. Dialysis method

h. USP dissolution method.

**2. In–Vivo Methods** Once the satisfactory in-vitro profile is achieved, it becomes necessary to conduct in-vivo evaluation and establish in-vitro in-vivo correlation. The various in-vivo evaluation methods are:-

a. Clinical response

b. Blood level data

c. Urinary excretion studies

d. Nutritional studies.

e. Toxicity studies

f. Radioactive tracer techniques

**3. Stability Studies:** Adequate stability data of the drug and its dosage form is essential to ensure the strength, safety, identity, quality, purity and in-vitro in-vivorelease rates that they claim to have at the time of use. A sustained release product should release a predetermined amount of the drug at specified time intervals, which should not change on storage. Any considerable deviation from the appropriate release would render the sustained release product useless. The in-vitro and in-vivo release rates of sustained release product may be altered by atmospheric or accelerated conditions such as temperature & humidity. The stability programmes of a sustained release product include storage at both nominal and accelerated conditions such as temperature & humidity to ensure that the product will withstand these conditions

**In vitro- In vivo Correlation:** The requirement of establishing good in-vitro invivo correlation in the development of sustained release delivery systems is self-evident. To make a meaningful in-vitro in-vivo correlation one has to consider not only the pharmaceutical aspect of sustained release drug delivery system but also the biopharmaceutics and pharmacokinetics of the therapeutic agent in the body after its release from the drug delivery system and also the pharmacodynamics of therapeutic agent at the site of drug action. A simple in vitro-in vitro relationship can be established by conducting in-vitro and in-vivo evaluations of a potential drug delivery system simultaneously to study and compare the mechanism and rate profiles of sustained drug release. When the in-vivo drug release mechanism is proven to be in good agreement with that observed in the in-vitro drug release studies, then in-vitro in-vivo correlation factor is derived. For capsule type drug delivery system the factor can be represented as:

Q= (Q/t) in vivo/ (Q/t) in vitro

Where Q/t = Rate of release ‘Q’ values are dependent profiles of drug delivery systems.Upon the sites of administration and environmental conditions to which the animals are exposed during treatment (study). The above relationship can be used for optimization of sustained release Levy has classified

**in-vivo – in-vitro correlation** in to: a) Pharmacological correlations based on clinical observations; b) Semi-quantitative correlations based on blood levels or urinary excretion data; c) Quantitative correlation arising from absorption kinetics. While most of the published correlations are of semiquantitative nature, the most valuable are those based on absorption kinetics.

**Bioavailability Testing:** Bioavailability is generally defined as the rate and extent of absorption of unchanged drug from its site of application to the general circulation. Bioavailability is defined in terms of a specific drug moiety, usually active therapeutic entity, which may be the unchanged drug or as with prodrug, for instance, a metabolite. In contrast, the term "absorption" often refers to net transport of drug related mass from its site of application into the body. Hence, a compound may be completely absorbed but only partially bioavailable as would occur, when low bioavailability is caused by incomplete absorption. Pharmaceutical optimization of the dosage form may be warranted to improve absorption characteristics of the drug and thereby also its bioavailability. Bioavailability studies are ordinarily single dose comparisons of tested drug product in normal adults in a fasting state. A crossover design, in which all subjects receive both, the product and reference material on different days is preferred. Guidelines for clinical testing have been published for multiple dose studies. Correlation of pharmacological activity or clinical evidence of therapeutic effectiveness with bioavailability may be necessary to validate the single significance of sustained release claims. While single dose studies are usually sufficient to establish the validity of sustained release dosage form design; multiple dose studies are required to establish optimum dosing regimen. They are also required when differencemay exist in the rate but not the extent of absorption. When there is excessive subject-tosubject variation or when the observed blood levels after a single dose are too low to be measured accurately. A sufficient number of doses must be administered to attain steady state blood levels. According to an extensive study of sustained release Theophylline products; for example, encapsulated forms showed less peaking during multiple dosing and therefore better control of blood level within the desired limits.

**Regulatory Requirements :** In India, the sustained release drug products in legal sense are considered to be "New Drugs" as per the Drugs and Cosmetic Act 1940, and Rules there under, 1945. The guidelines and requirements are given under the schedule 'Y.